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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/088,269

09/16/2002

Olli P. Kallioniemi

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01/04/2005

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EXAMINER

DEJONG, ERIC S

ART UNIT

PAPER NUMBER

1631

DATE MAILED: 01/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/088,269

Applicant(s)

KALLIONIEMI ET AL.

Examiner

Eric S. DeJong

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 15 March 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-40 and 58-63 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) \_\_\_\_\_ is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-40 and 58-63 are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

The communication by applicant filed on 15 March, 2002 containing amendments to the specification and claims is acknowledged. Amended claims 1, 15, and 24 and the cancellation without prejudice of claims 41-57 are acknowledged.

### ***Lack of Unity***

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-40, drawn to a computer implemented method of counting nucleic acid probe signals in a region of interest of a biological specimen comprising counting signals from test and reference probes and determining a ratio of counted test signals to the counted reference probes. If this group is elected then the summarized species election below is required.

Group II, claim(s) 58 and 59, a computer-readable medium comprising computer-executable instructions for projecting possible fluorescent image components within a stack of image slices generated from a plurality of confocal microscopic observations of a FISH experiment, discarding insignificant contiguous fluorescent image components,

grouping specific regions into spot candidates, applying a filter to spot candidates and counting the remaining candidates as spots.

Group III, claim(s) 60-63, drawn to a computer-generated user interface for presenting results of microscopic observation of biological tissue subjected to a FISH experiment as a scatter plot where points indicate spot size and intensity.

The inventions listed as Groups I-III do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding technical features for the following reasons:

The single common concept between the inventions of Groups I-III is the observation of signals from hybridized probes within biological samples and is already well known in the art. See Garini et al., Abstract. Therefore, the special technical feature linking the inventions of groups I-III does not constitute a special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art.

The special technical feature of Group I is considered to be a method of computer-implemented counting nucleic acid probe signals in a region of interest in a biological specimen comprising in a computer system, automatically counting a number of test signal probes from a test probe, in the computer system, automatically counting a number of reference signals from a reference probe, and in the computer system, determining a ratio of the automatically-counted test signals from the test probe to the automatically-counted reference signals from the reference probe wherein the region of interest comprises multiple cells.

The special technical feature of Group II is considered to be a computer readable medium comprising computer-executable instructions for performing the following: within a stack of image slices generated from a plurality of confocal microscopic observations of a FISH experiment as a plurality of depths along a z-axis, identifying possible fluorescent image components, projecting the possible fluorescent image components within the image slices onto a projection image, discarding insignificant contiguous possible fluorescent image components in the slice, for each contiguous region in the projection image grouping regions of possible fluorescent image components associated with the contiguous region in the projection image into spot candidates, applying a filter to the spot candidates, and counting the remaining spot candidates as spots.

The special technical feature of Group III is considered to be a computer generated interface for presenting results of microscopic observations of biological tissue subjected to a FISH experiment comprising a scatter plot of sets of image components designated as spot candidates for the FISH experiment wherein the scatter plot comprises points indicating a size and intensity of spot candidates.

### **SPECIES ELECTION FOR GROUP I**

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

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Species of a computer implemented method of counting nucleic acid probe signals in a region of interest of a biological specimen as set forth in claim 15 is independent and separately published in literature thus demonstrating an undue burden if searched together with a method comprising additional generic steps. Applicant is to elect a single disclosed specie of a computer implemented method of counting nucleic acid probe signals: a method further comprising (A) an addition method step of counting visible signals from probes used in *in situ* hybridization of biological of a biological sample comprising obtaining a plurality of images, construction of a three-dimensional model, and counting discrete signals at different levels of the three dimensional model, or (B) an unspecified method step with respect to that listed above.

Applicant is required, in the reply to this action, to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1-14 are generic.

If applicant selects above specie (A) then the following sub-species election is required.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

Species of a method of counting visible signals from probes used in *in situ* hybridization of a biological sample as set forth in claims 21, 28, 29, 30, 31, 33, 37, 38,

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39 and 40 are independent and separately published in literature thus demonstrating an undue burden if searched together. Applicant is to elect a single disclosed specie of a method for counting visible signals from probes used in *in situ* hybridization of biological samples: a method further comprising (C) determining a ratio between the test signals and the reference signals, (D) avoiding counting signals having intensities exceeding a threshold intensity, (E) avoiding counting discrete signals related to autofluorescent material, (F) identifying a set of one or more discrete signals as a cluster and counting the cluster as a number of discrete signals greater than the number of discrete signals in the set, (G) avoiding counting discrete signals appearing at the same location in the set of images for the first color channel and the set of images for the second color channel, (H) avoiding counting discrete signals appearing at the same location in the set of images for the test probe and the set of images for the reference probe, (I) receiving a directive from a user indicating counting is to be avoided for a specified portion of the biological sample and responsive to the directive, avoiding counting discrete signals for the specified portion of the biological sample, (J) receiving a directive from a user indicating counting is to be performed separately for a specified portion of the biological sample and responsive to the directive separately counting discrete signals for the specified portion of the biological sample, or (K) an unspecified method step with respect to those listed above.

Applicant is required, in the reply to this action, to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 15-20 and 23-27 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. DeJong whose telephone number is (571) 272-



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6099. The examiner can normally be reached during the hours 8:30AM-5:00PM on Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-0722. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

EDJ



 1/3/05  
ARDIN H. MARSCHEL  
PRIMARY EXAMINER